REMARKS

Status of the Claims

Claims 18-20 have been added with this amendment and contain no new matter. Claims 1-20 are pending.

Specification

The status of the parent application Serial No. 09/776,426 has been updated to include the corresponding Patent No. 6,638,973, as requested by the Office.

Rejection Under 35 U.S.C. § 112, First Paragraph

Reconsideration is respectfully requested of the rejection of claims 1-17 under 35 U.S.C. § 112, first paragraph for the lack of enablement as alleged by the Office. More specifically, the Office noted that the specification does not provide enablement for the broad number of cancers embraced by the claims. However, the Office noted that the taxanes of the present invention exhibit activity against ovarian cancer, and have promising activity against breast, head, neck, esophageal, and lung cancer. Furthermore, Examples 5, 25, 30, and 41 describe the efficacy of the taxanes of the present invention, i.e., the taxanes having a solubility in ethanol at room temperature of at least 200 mg/ml against a human colon cancer cell line HCT116. Accordingly, "a neoplastic cancer" has been amended to "a cancer selected from the group consisting of breast, head, neck, esophageal, lung, and colon cancer." In view of the amendment, claims 1-17 satisfy the enablement requirement, and respectfully request withdrawal of the enablement rejection.

Rejection under 35 U.S.C. § 112, Second Paragraph

Reconsideration is requested of the rejection of claims 1-2, and 4-17 as being indefinite for failing to particularly point out and distinctly claim the subject matter, which applicant regards as the invention.

The Office alleged that the term "ethanol" in claim 1 and the term "the HCT116 cell line" in claims 7-9 and 12-17 have insufficient antecedent basis. Applicants respectfully disagree.

As stated in MPEP 2173.05(a), "[T]he meaning of every term used in a claim should be apparent from the prior art or from the specification and drawings at the time the application is filed. Furthermore, as stated in MPEP 2173.05(d),

> [t]he failure to provide explicit antecedent basis for terms does not always render a claim indefinite. If the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite. Ex parte Porter, 25 USPQ2d 1144,1145 (Bd. Pat. App. & Inter. 1992).

It was known in the prior art that taxanes such as paclitaxel were water-insoluble and were soluble in ethanol to a certain degree. In addition, the specification discusses the solubility of taxanes in ethanol in significant detail. By way of example, the specification states that ethanol is the preferred solvent for use in dissolving the antitumor compounds of the present invention (see page 43, lines 28-29). Furthermore, examples 42 and 46 describe 11 solutions and 3 solutions, respectively, wherein taxanes were dissolved in ethanol, and example 45 describes 3 such emulsions. Accordingly, the meaning of the term "ethanol" in claim 1 is **not** indefinite in view of the prior art and the specification.

With regard to "**the** HCT116 cell line", this term has been amended to " an HCT116 cell line." Numerous pieces of prior art discuss the use of this cell line, which is a human colon adenocarcinoma that can be used to study cytotoxic effects of a number of drugs. Additionally, Examples 5, 25, 30, and 41 discuss the use of HCT116 cells in cell survival tests performed with a number of taxane compounds of the present invention. In view of the above, the term "an HCT116 cell line" is **not** indefinite.

Rejection Under 35 U.S.C. § 103(a)

Reconsideration is requested of the rejection of claims 1-17 under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,395,770 (Broder et al.) and US Patent

Application No. 2001/0029264 (McChesney-Harris) in view of Goodman & Gilman's, The Pharmacological Basis of Therapeutics, Ninth Edition.

Broder et al. describe a method for making an orally administrable taxane bioavailable to human patients at a level sufficient to treat taxane-responsive conditions by orally co-administering a taxane comprising a derivative or analog of paclitaxel or docetaxel and an oral bioavailability enhancing agent comprising a cyclosporin. The liquid taxane preparations described in Broder et al. include paclitaxel or other taxane in a vehicle comprising CREMOPHOR® EL or other polyethoxylated castor oil, alcohol and/or a polyoxyethylated sorbitan mono-oleate, with or without flavoring. Furthermore, each dosage form includes an effective amount of a taxane target agent (e.g. Cyclosporin A) and pharmaceutically inert ingredients, such as excipients. See column 12, lines 12-22.

McChesney-Harris describes compositions for treating taxane-responsive conditions consisting of: 1) paclitaxel, CREMOPHOR® EL/citric acid blend, dimethylisosorbide (DMI), and vitamin E-TPGS, and 2) paclitaxel, ethanol, citric acid, and vitamin E-TPGS (see Tables 1 and 7).

Goodman and Gillman disclose that paclitaxel has very limited solubility and must be administered in a vehicle of 50% ethanol and 50% polyethoxyethylated castor oil. Goodman and Gillman do not address oral administration of taxanes; rather, they only discuss the administration of paclitaxel in the form of infusions.

As amended herewith, claim 1 is directed to a method of treating a patient afflicted with a cancer selected from the group consisting of breast, head, neck, esophageal, lung, and colon cancer by orally administering a pharmaceutical composition consisting essentially of a taxane, a solvent capable of dissolving the taxane, polyoxyethylatated castor oil, a diluent, and optionally a flavoring, wherein the taxane has a solubility in ethanol at room temperature of at least 200 mg/ml.

Accordingly, the method of claim 1 requires use of a taxane having a solubility in ethanol at room temperature of at least 200 mg/ml. In contrast, Broder et al. and McChesney-Harris merely disclose formulations containing taxol (also known as

paclitaxel). Taxol, however, does not have a solubility of ethanol of at least 200 mg/ml; rather, the solubility of taxol in ethanol is less than 40 mg/ml.[1] Furthermore, Broder et al., McChesney-Harris, and Goodman and Gillman do not suggest that any advantages could be derived by selecting a taxane having a solubility in ethanol which is substantially greater than the solubility of taxol in ethanol.

With all due respect, the Office has not established a *prima facie* case of obviousness with respect to claim 1. The three references, either alone or in combination, do not disclose or suggest the preparation of pharmaceutical compositions containing a taxane having a solubility in ethanol which is significantly greater than the solubility of taxol in ethanol. In view of the above, withdrawal of the obviousness rejection is requested.

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[1]TAXOL Science and Applications, Edited by Matthew Suffness, CRC Press, ISBN0-8493-8382-X, Chapter 9 Biopharmaceutics of paclitaxel (taxol): Formulation, activity, and pharmacokinetics, page 238, written by Robert Straubinger

CONCLUSION

In light of the foregoing, Applicants request entry of the claim amendments, withdrawal of the claim rejections, and solicit an allowance of the claims. The Examiner is invited to contact the undersigned attorney should any issues remain unresolved.

Enclosed is a check for $110 for a one month extension of time. The Commissioner is hereby authorized to charge any underpayment and credit any overpayment of government fees to Deposit Account No. 19-1345.

Respectfully submitted,

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